

ABSTRACT

Drug induced cardiotoxicity have emerged as an important factor for developing cardiovascular complications. Present day therapeutics for various lifestyle diseases including cancer, diabetes and obesity are reported to have cardiotoxic side effects and require urgent attention of the scientific community. Use of natural bioactive compounds having cardioprotective properties for supplementing cardiotoxic therapies holds a great potential in this regard. This will improve the cardiac health without compromising the therapeutic efficiency of the drugs. With this in mind, the present study was designed to analyze the effects of Curcumin, polyphenol derived from *Curcuma longa* and well-known for broad range of protective effects, in drug induced cardiotoxicity. Two different classes of drugs with known cardiotoxicity were selected for the study with applications in cardiac (hypotension) and non-cardiac (cancer) conditions, namely Levophed (or Norepinephrine or NE) and Doxorubicin, respectively.

Cardiotoxic stress induced by these drugs was firstly confirmed on cardiomyoblasts in concentration and time dependent manner by various cell viability assays individually. The effects of Curcumin on Doxorubicin and Levophed induced cardiotoxicity were then studied by various microscopic, molecular, biochemical and immunological assays. *In silico* molecular docking studies were conducted for Doxorubicin, NE and Curcumin with signaling molecules reported in different cardiac stresses to derive the possible signaling involved in Curcumin mediated effects. Gene expression analysis was done at transcriptomic and proteomic levels for various cell survival and death biomarkers in drug induced *in vitro* and *in vivo* models treated with Curcumin at different time points.

We observed that both the selected drugs results in dose mediated stress responses in cardiomyoblasts and Curcumin significantly resisted and prevented these effects in a mode dependent manner. The *in vitro* findings were validated in *in vivo* models and possible signaling mechanism of Curcumin mediated effects were derived.

In conclusion, Curcumin holds a great potential for reducing drug induced cardiotoxicity when supplemented with the ongoing therapies having cardiotoxic effects.